Centers for Disease Control and Prevention Draft November 22, 2002

ANNEX 10

Smallpox Fact Sheet

Smallpox Vaccination Program Guidance: Annex 10
SMALLPOX FACT SHEET

Key Facts Resource

Definition

smallpox (variola); an acute, contagious and sometimes fatal disease caused by orthopoxvirus and marked by fever and a distinctive progressive skin rash. Smallpox was declared eradicated in 1980 following worldwide vaccination programs.

Smallpox Forms and Presentation

There are two forms of smallpox (variola): variola major and variola minor (or alastrim).

- *variola major*: Severe, with extensive rash, higher fever, 30% fatality
- *variola minor*: Much less severe, 1% or less fatality

There are four clinical presentations of *variola major* in unvaccinated persons:

- ordinary: Most frequent (occurs in 90% or more of all cases)
- modified: Mild, occurring in previously vaccinated persons
- flat: Severe and uncommon; usually fatal
- hemorrhagic: Severe and uncommon; usually fatal

Characteristics of Ordinary Smallpox

Transmission: Smallpox most often is transmitted through direct and fairly prolonged face-to-face contact with an infected person. While far less common, smallpox also can be spread through contact with infected bodily fluids or contaminated objects such as bedding or clothing. Rarely, smallpox has been spread by airborne virus in enclosed settings such as buildings or buses. Smallpox is not known to be transmitted by insects or animals.

Incubation Period: After exposure, it may take between 7 and 17 days (average 12 to 14) for symptoms of smallpox to appear. During this time, the infected person feels fine and is not contagious.

Symptoms: Symptoms begin with high fever, head and body aches, and sometimes vomiting. A rash follows that begins in the mouth first, then quickly spreads to the body and progresses to raised bumps that crust, scab, and fall off after about three weeks, leaving a pitted scar.

Appearance: The rash emerges first as small red spots on the tongue and in the mouth. It next appears on the skin, starting on the face and then spreading to the arms and legs and then to the hands and feet. The rash becomes raised bumps, which fill with a thick, opaque fluid and often have a depression in the center that looks like a belly-button. The bumps become pustules—sharply raised, usually round and firm to the touch. The pustules form a crust and then scab.

Contagion: A person is contagious once a rash appears and until the last smallpox scab falls off.

Smallpox as a Bioweapon

- Smallpox is classified as a Category A agent by the Centers for Disease Control and Prevention. Category A agents are those that pose the greatest potential threat for adverse public health impact, have a moderate to high potential for large-scale dissemination or a heightened general public awareness and require broad-based public health preparedness efforts. Other Category A agents are anthrax, plague, botulism, tularemia and viral hemorrhagic fevers.
- The deliberate release of smallpox as an epidemic disease is now regarded as a possibility.
- One suspected case of smallpox is considered a public health emergency.

Treatment

There is no proven treatment for smallpox, but research to evaluate new antiviral agents is ongoing and there have been some very initial results with the drug cidofovir that suggest it may be useful. Patients with smallpox can benefit from supportive therapy (e.g., intravenous fluids, medicine to control fever or pain) and antibiotics for any secondary bacterial infections that may occur. Smallpox can be prevented through the smallpox vaccine. [Note: The use of cidofovir to treat smallpox or smallpox vaccine reactions is experimental and should be evaluated and monitored by experts at NIH and CDC.]

Smallpox Vaccine

The smallpox vaccine prevents smallpox. It provides full immunity for 3 to 5 years and decreasing immunity thereafter. People vaccinated decades before may retain some smallpox immunity, but it is not known how much.

The smallpox vaccine is made from a related, milder virus called **vaccinia**. When administered in a vaccine, the vaccinia virus helps the body develop immunity to smallpox. This is a “live virus” vaccine, meaning that the vaccinia virus is live in the vaccine and, once administered, live at the vaccination site so the site must be cared for carefully to prevent vaccinia virus from spreading. The smallpox vaccine does not contain the smallpox virus and cannot cause smallpox.

The vaccinia virus may cause rash, fever, and head and body aches. Vaccinia does not cause smallpox. Vaccinia is spread by touching a vaccination site before it has healed or by touching bandages or clothing that have become contaminated with live virus from the vaccination site. In the past, most complications of this type occurred in the vaccinees themselves. Spread to other individuals almost always occurred with intimate contact such as occurs in the household. In the past, spread of vaccinia virus to contacts was reported to occur about 27 times in 1 million vaccinees. Vaccinia has not been shown to spread through airborne contagion like smallpox.

The vaccine is given using a two-pronged needle that is dipped into the vaccine and then used to quickly prick the skin a number of times. The pricks are not deep but will cause a small sore spot and droplets of blood to form. The vaccine usually is given in the upper arm.

The vaccine can have side effects ranging from normal and typically mild reactions to potentially life-threatening reactions causing death. Reactions are fewer and less severe in previously vaccinated people.

Vaccine Reactions

- Most people experience **normal, usually mild reactions** that include a sore arm, fever, and body aches. In recent tests, one in three people felt bad enough to miss work, school, recreational activities, or had trouble sleeping after receiving the vaccine.
- In the past, about 1,000 people for every 1 million people vaccinated for the first time experienced reactions that, while not life-threatening, were **serious**. These types of reactions include a toxic or allergic reaction at the site of the vaccination (erythema multiforma), contact spread of the vaccinia virus to other parts of the body or to other individuals (inadvertent inoculation) and spread

Note

of the vaccinia virus to other parts of the body through the blood (generalized vaccinia). These types of reactions may require medical attention.

- In the past, between 14 and 52 people out of every 1 million people vaccinated for the first time experienced potentially **life-threatening reactions** to the smallpox vaccine. These reactions included serious skin rashes caused by widespread infection of the skin (eczema vaccinatum), ongoing infection of the skin with tissue destruction (progressive vaccinia or vaccinia necrosum) and inflammation of the brain (postvaccinal encephalitis). These reactions require immediate medical attention.
- From past experience, it is estimated that one or two people in 1 million who receive the vaccine the first time may die as a result.

(See "Adverse Event Rates" chart at the end of this Fact Sheet for more detailed information.)

Contraindications to Vaccine

Some people are more likely to have serious reactions to the vaccine. People most likely to have side effects include: people who now have, or have had, skin conditions (especially eczema and atopic dermatitis); people with weakened immune systems, such as those who have received a transplant, are HIV positive, or are receiving treatment for cancer or are currently taking medications like steroids that suppress the immune system. Also, women who are pregnant should not receive the vaccine because of the risk it poses to the fetus. Also, individuals under 18 years of age and those allergic to the vaccine or any of its components should not receive the vaccine.

All those listed above should **NOT** receive the vaccine **unless** they have been exposed to smallpox.

Careful screening of potential vaccine recipients is essential to minimize the number of adverse reactions.

A Note on Today's Adverse Event Rates

Statistical information about smallpox vaccine adverse reactions is based on data from two studies conducted in 1968. Adverse events in the United States today may be higher because there may be more persons at risk from 1) immune suppression from cancer, cancer therapy, organ transplantation and other illnesses, such as HIV/AIDS, and 2) eczema or atopic dermatitis. The outcome associated with adverse events may be less severe than previously reported because of advances in medical care. Rates may be lower for persons previously vaccinated.

Vaccine Availability

Right now, the U.S. government has access to enough smallpox vaccine to effectively respond to a smallpox outbreak in the United States. An unlicensed, diluted vaccine would likely need to be used in the eventuality of a large outbreak. Testing has shown that existing supplies of vaccine could be diluted by a 1 to 5 ratio and still remain as effective and safe as full-strength vaccine. This dilution would result in 75 million doses of Dryvax.

As of November 1, 2002, two lots of the Dryvax vaccine (2.7 million doses) are approved for distribution as a licensed vaccine. One million doses are designated for the Department of Defense. The remaining 1.7 million doses are designated for the Department of Health and Human Services.

All remaining existing vaccine supply is currently unlicensed. Additional Dryvax vaccine may undergo licensure. The Aventis Pasteur vaccine is vaccine from

Smallpox Vaccine Supply:

Existing Supply:

- Dryvax: 15 million doses *(2.7 million doses are approved for distribution as a licensed vaccine)*
- Aventis Pasteur: 85 million doses

In Production:

- Acam 1000: 54 million doses due May, 2003
- Acam 2000: 155 million doses due May, 2003

(Note; In an emergency, the 15 million doses of Dryvax could be diluted (X5) to produce 75 million doses)

1950s that can be used in the event of an emergency.

In addition, new supplies of smallpox vaccine (Acam) are being produced and are expected to be licensed.

Treatment of Adverse Reactions

Two treatments may help people who have certain serious reactions to the smallpox vaccine. These are vaccinia immune globulin (VIG) and cidofovir. Currently there are 700 doses of VIG on hand (enough for 6 million people vaccinated), and 3,500 doses of cidofovir (enough for at least 15 million people vaccinated). (See note on cidofovir.) Additional doses of VIG are being produced, and measures are underway to increase supplies of cidofovir as well.

Important Dates

1796 Edward Jenner demonstrated that smallpox could be prevented by inoculation with material from a cowpox lesion.
1949 Last case of smallpox in the United States occurred in Texas.
1966 World Health Organization began intensified global smallpox eradications program.
1972 Routine smallpox immunization of the American public stopped.
1977 Last naturally occurring case of smallpox in the world occurred in Somalia.
1978 Last cases of smallpox occurred in the United Kingdom as a result of a laboratory accident.
1980 World Health Assembly officially certified the global eradication of smallpox.

Interesting Facts

- Smallpox is believed to have emerged in human populations about 10,000 BC.
- All poxviruses like smallpox are rapidly inactivated by exposure to ultraviolet light and chemical disinfectants such as bleach or Lysol.
- In laboratory experiments, 90% of aerosolized smallpox virus dies within 24 hours; in the presence of ultraviolet (UV) light, this percentage would be even greater.
- The variola virus remains infectious in smallpox scabs for years, but because the virus is encased in a fibrin matrix transmission is rare from such scabs.

Smallpox Vaccine
Adverse Event Rates, 1968
(number per million vacinees)

	NATIONAL SURVEY		TEN STATE SURVEY	
	All primary vaccinees	Vaccinees ≥ 1 yr old	All primary vaccinees	Vaccinees ≥ 1 yr old
Serious, but not life-threatening reactions:				
Inadvertent Inoculation	25.4	27.1	529.2	532.0
Generalized Vaccinia	23.4	17.7	241.5	222.8
Erythema Multiforme	Not Available	Not Available	164.6	131.3
Total number of serious, but not life-threatening reactions:	**48.8**		**935.3**	
Life-threatening reactions:				
Postvaccinal Encephalitis	2.9	2.4	12.3	8.6
Progressive Vaccinia (Vaccinia Necrosum)	.9	1.0	1.5	1.7
Eczema Vaccinatum	10.4	10.6	38.5	41.5
Total number of life-threatening reactions:	14.2		52.3	
Deaths:	1.1	.6	None Reported	None Reported

This table presents smallpox vaccine adverse event rates from two studies done in 1968 (see references below). The two studies were carried out using different methodologies. In the national survey, information was gathered from seven nationwide sources, with most of the information on adverse reactions coming from the American Red Cross Vaccinia Immune Globulin (VIG) distribution system. Reactions that did not require use of VIG (that is, less severe reactions) are less likely to be reported through this system. In the ten state survey on the other hand, doctors were directly surveyed to report all adverse reactions, even those considered less severe. For this reason, the ten-state survey data may present a better estimate of the number of people having adverse reactions to the vaccine.
Note: Adverse event statistics cited in document are highlighted.

1. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccinations, 1968: national surveillance in the United States. New Engl J Med 1969;281:1201-1208.
2. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: results of ten statewide surveys. J Infect Dis 1970;122:303-309.

For more information, visit www.cdc.gov/smallpox, or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)

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